

REMARKS/ARGUMENTS

Claims 1-2, 5, 8, 10-12, 24 and 26-27 are active. Claims 3-4 and 25 and non-elected claims 17-18 have been cancelled without prejudice. Independent claim 1 has been directed to detection of the expression of Bax or Bak protein. Consistent amendments to the dependent claims have been made. New claims 25-26 find support in the original elected claims 1, 5, and 8 and on page 8, lines 17 *ff.* of the specification. Claims 6, 7, 9, and 13 and 17-23 were previously withdrawn from consideration.

Restriction/Election

The Applicants previously elected with traverse Group I as directed to a process of *in vitro* detection of resistant cancer cells to oxaliplatin treatment and to the following species: colorectal cancer, Bax and TNF. The Requirement has now been made FINAL. The Applicants respectfully request rejoinder and examination of any non-elected species upon an indication of allowability for a generic claim reading on the elected species. Rejoinder of claims in the non-elected groups which depend from or otherwise include all the limitation of an allowed elected claim is also respectfully requested, MPEP 821.04.

Rejection—35 U.S.C. §112, second paragraph

Claims 1-3 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. These rejection is moot in view of the amendments above.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-5, 8 and 10-12 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. This rejection may be withdrawn in view of the amendment of independent claim 1 above.

Rejection—35 U.S.C. §102

Claims 1-5 and 8 were rejected under 35 U.S.C. 102(b) as being anticipated by Macpherson et al, Proc. Am Assoc Canc. Res. 43:407. Macpherson does not anticipate the invention because it does not disclose that elevated expression of genes encoding the pro-apoptotic proteins Bax and Bak correlate with oxaliplatin resistance. That is, that cells expressing high levels of Bax and Bak are sensitive to oxaliplatin, while those expressing low levels are more resistant, see e.g., Example 2 on page 33 *ff.* of the specification.

On the other hand, MacPherson involves “**Bcl-xl**. . .an anti-apoptotic member of the Bcl-2 family”. MacPherson indicates that cells in which Bcl-xl function was knocked out become sensitive to oxaliplatin via an apoptotic mechanism. However, there is no teaching in MacPherson that lower levels of the pro-apoptotic **Bax** and **Bak** proteins exemplified in the specification, correlate with oxaliplatin resistance. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Objection

The specification or claim 11 was objected to as containing a typographical error. This objection is now moot.

Rejection—35 U.S.C. §112, second paragraph

Claims 24-25 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the amendment of claim 24 and the cancellation of claim 25.

Rejection—35 U.S.C. §112, first paragraph

Claim 25 was rejected under 35 U.S.C. 112, first paragraph, as lacking adequate description. This rejection is moot in view of the cancellation of this claim.

Rejection—35 U.S.C. §102(a)

Claim 24 was rejected under 35 U.S.C. 102(a) as being anticipated by Gordier, et al., FEBS Lett. 529:232. This rejection is moot in view of the attached certified translation of the priority document, FR 02/07417.

Support for claim 24 (detection of the Bax gene expression in colorectal cancer cells) is found in the priority document. In the certified translation it is indicated that the HCT116R line (a colorectal cancer cell line) does not express the Bax protein (see legend for fig. 1, page 23, lines 16-18 and page 26, lines 8-9) and are resistant to oxaliplatin treatment (page 26, lines 30-32 and page 27, lines 1-16).

Rejection—35 U.S.C. §103(a)

Claims 1-5, 8 and 10-12 were rejected under 35 U.S.C. §103(a) as being unpatentable over Macpherson, et al. Proc. Am Assoc Canc. Res. 43:407, as applied to claims 1-5 and 8 above, and further in view of Liu, et al., Clin. Canc. Res. 3: 2039. MacPherson has been discussed above and does not disclose or suggest that reduced expression of Bax or Bak correlate with oxaliplatin resistance as shown by the inventors, see e.g., Example 2. Liu was cited as disclosing a PCR-based method for detecting Bcl-xl (an anti-apoptotic protein). Liu also refers to the pro-apoptotic protein Bax (see abstract). However, like MacPherson, Liu does not disclose that reduced expression of Bax or Bak correlate with oxaliplatin resistance. Accordingly, this rejection may now be withdrawn.

Conclusion

In view of the amendments and remarks above, the Applicants respectfully submit that this application is now in condition for allowance. An early notice to that effect is earnestly solicited.

Respectfully submitted,

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